CHAPTER–I

ⓐ INTRODUCTION

ⓑ CHLORAMINE-T

ⓒ LITERATURE SURVEY.

ⓓ OBJECT AND SCOPE OF THE WORK.

a) INTRODUCTION

The study of chemical phenomena can be made from two fundamental approaches. The first of these is known as 'Thermodynamics'. It is a vigorous and exact method concerned with equilibrium conditions of final and initial states of chemical changes. The other method is known as "Kinetics". It is less vigorous and deals with a more complex aspect of chemical phenomena namely the rate of change from initial to final states under nonequilibrium conditions. The importance of the study of kinetics is in chemical changes. It furnishes information not only about the final products formed but also about the intermediates formed during the course of the reaction. These intermediates are though short lived, are responsible for controlling the over all reaction.

The mechanism of chemical reaction may be considered as a hypothetical motion picture of the behaviour of the participating atoms. Such a picture would begin at some time before the reacting species approach each other, then go on to record the continuous paths of the atoms during the course of reaction. Thus the mechanism is the actual process by means of which a reaction takes place, involving the information, such as which bonds are broken, in what order, how many steps are involved, the relative rate of each step and similar important points.

It is well established fact that a chemical reaction takes place at a certain rate under a particular set of conditions such as temperature, pressure, concentration of species and presence or absence of catalysts. All the reactions under similar conditions do not proceed at the same rate. The study of reaction rates, which forms the field of chemical kinetics, is of considerable importance to analytical and industrial chemists. With the help of the knowledge of "kinetics of system", one can increase or decrease the rate of reaction by changing the conditions used.

The rate of reaction is determined by the mathematical expression showing the dependance of rate on the concentration of the reactants. In some reactions the change occurs directly, which may be represented by an overall stoichiometric equation. In complex reaction the substances undergo a series of stepwise changes. The over all mechanism is then made up of contributions from all such reactions. For example see this reaction

$$2A + B \longrightarrow C + D$$

might take place as follows -

$$A + B \rightleftharpoons AB \qquad \text{Step I}$$

$$A + AB \rightleftharpoons A_2B \qquad \text{Step II}$$

$$A_2B \rightleftharpoons AB + C \qquad \text{Step III}$$

$$AB \rightleftharpoons D \qquad \text{Step IV}$$

$$2A + B \rightleftharpoons C + D$$

The slowest step among these controls the rate of the over all reaction and may be determined from the rate equation. The mechanism rather than the rate equation is important to theoretical chemists.

The theories put forth by different scientists in this connection are summarised and now-a-days two theories have been accepted to explain the organic reactions. The first theory is known as "the collision theory or the theory of absolute reaction rate." It is based upon the energy of activation of the rate determining factor. This may be related to the temperature (T) and rate constant (k) by a modified form of the Arrhenius equation :

$$k = p.z.e^{-Ea/RT}$$

where

k = Rate constant,

p = Probability factor,

z = Frequency of collision at unit concentration,

Ea = Energy of activation,

T = Absolute temperature

and R = Gas constant.

The last term accounts for considerable deviation in some cases between theory and experimental results. The value of 'z' can be calculated from the kinetic theory.

The second theory is called as "transition state theory", which is also put forth to explain the reaction kinetics. According to this theory, any molecule undergoing reaction must form an activated complex in equilibrium with the reactants and then the decomposition of the complex to form the products. For reaction between A and B these two steps can be represented by following equation

$$A + B \rightleftharpoons AB^{*} \longrightarrow \text{products}$$

* Activated complex.

Since the rate of reaction is proportional to [AB*], the specific rate [$kr = \frac{\text{rate}}{(A)x(B)}$] for the reaction should be proportional to $K^{\neq}$ [equilibrium constant]. Further, we can show that the proportionality constant is very close to KT/h. Where K is Boltzmann's constant, 'T' is the absolute temperature and 'h' is the plank's constant. The transition state theory is analogous to corresponding thermodynamic functions of ordinary chemical changes.

The free energy of activation $\Delta G^{\neq}$

$$\Delta G^{\neq} = -RT \ln K^{\neq} = -RT \ln \left[\frac{k_r h}{KT}\right]$$

The heat of activation ($\Delta H^{\neq}$) or enthalpy of activation.

$$\Delta H^{\neq} = -R \frac{d(\ln K^{\neq})}{d(1/T)} = -R \left[\frac{d(\ln kr)}{d(1/T)} + T\right]$$

The entropy of activation, $\Delta S^{\neq}$

$$\Delta S^{\neq} = \frac{\Delta H^{\neq} - \Delta G^{\neq}}{T} = R\left[T \frac{d(\ln kr)}{d_T} + \frac{\ln krh}{KT} - 1\right]$$

Entropy of Activation :

Entropy is the measurement of randomness of a system. If a reaction occurs with an increase in entropy, there is a disorder possible more among the products than the reactants or it is a measure of the

freedom from restrictions to the motion of the reactant[2] molecules than to the product molecules.

The entropy of activation may be calculated by equation

$$\Delta S^{\neq} = \frac{\Delta H^{\neq} - \Delta G^{\neq}}{T}$$

Long et.al. (1957),[3] amplifying a suggestion of Taft and coworkers,[4] have proposed the use of ΔS^* as criteria of the mechanism of hydrolysis reaction. The reactions are usually classified as unimolecular (A-1, SN^1) or bimolecular (A-2, SN^2). In the former case, a water molecule does not participate in the rate determining step. The A-1 and A-2 processes involve specific hydronium ion catalysis and may be represented as follows.[5]

$$S + H^+ \underset{\text{fast}}{\rightleftharpoons} SH^+$$

$$SH^+ \xrightarrow{\text{slow}} \text{products (A-1)}$$

$$S + H^+ \underset{\text{fast}}{\rightleftharpoons} SH^+$$

$$SH^+ \xrightarrow[H_2O]{\text{slow}} [X^{\neq}] \xrightarrow{\text{fast}} \text{products (A-2)}$$

Activated complex

It seems quite reasonable that the loss of transitional and rotational freedom of water molecule associated with the bimolecular process, should lead to lower entropy of activation relatively to unimolecular process

It can be said that if the entropy of activation is negative then the mechanism is probably bimolecular. Emphirically all known bimolecular reactions specifically acid-catalysed reactions, have negative entropy of activation and all known unimolecular acid catalysed reactions have entropy of activation nearly zero or above.

Solvent Effect :

The change in the solvent will affect both the rate and the mechanism of reaction. Sometimes the solvent alters the rate without affecting the mechanism and rarely changes the mechanism without altering the rate. The most pronounced effects of solvents are observed for reactions between ions and for those in which the ions are generated from uncharged molecules. Reactions, in which the charge is created, proceed most rapidly in polar solvents.[3]

The theory put forward by Hughes and Ingold[6] could be used as criteria to understand the mechanism. According to this theory an increase in ionisation power of solvent will favour an increase in the magnitude of charge.

Ionic Strength Effect :

The reaction between two ionic species proceeds through transition state, which is in equilibrium with reactants. The equilibrium properties of such reactions can be greatly affected by the other ionic species, which may be present in addition to the reactants.

The variable that determines the effect of ion on the equilibrium is the ionic strength and it is defined by equation

$$\mu = \frac{1}{2} \Sigma \, m_i Z_i^2$$

where m_i = molality of the ion and

Z_i = charge of ion.

The effect of electrostatic interaction of ionic species can be successfully treated by activity rate theory which was developed by Brönsted, Bjerrum and Debye-Hückel.

The theoretical rates can be calculated by applying second empirical equation of Debye-Hückel and can be compared with observed rates as has been done for the hydrolysis of propionamide.[7]

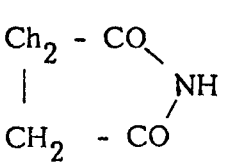
b) CHLORAMINE-T (A Reagent)

$[P\text{-}CH_3.C_6H_4.SO_2NClNa]$

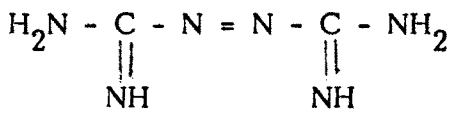
Chloramines are compounds in which one or more chlorine atoms are attached to nitrogen. Organic chloramines are N-chloro derivatives of following groups of compounds.

i) Sulphonamides $R\text{-}SO_2.NH_2$

ii) Heterocyclic chloramines with chlorine attached to nitrogen in the ring



iii) Condensed amines from cyanamide derivatives.



iv) Anilides

$C_6H_5NH.CO.CH_3$

Organic chloramines are prepared by well known method.[8] Commercial chloramines such as chloramine-T and chloramine-B are used as antiseptic and disinfectant reagents in tooth-pastes, soaps and in the treatment of infected wounds.

Chlorine atom bonded to nitrogen in chloramines is positive with an oxidation state +1, so all compounds containing N-Cl group liberate iodine in acidified potassium iodide solution. The over all reaction for monochloramines can be written as

$$RR'N\text{-}Cl + 2I^- + H^+ \longrightarrow RR'NH + I_2 + Cl^-$$

Fairly stable organic dichloramine-T (DCT) also reacts with acidified potassium iodide solution with evolution of iodine.

$$RNCl_2 + 4I^- + 2H^+ \longrightarrow R\text{-}NH_2 + 2I_2 + 2\overline{Cl}$$

From the analytical point of view, the most important class of chloramines is perhaps the N-Chloro derivatives of aromatic sulphonamides.

Chloramine-T [$P\text{-}CH_3.C_6H_4SO_2NCl\ Na,\ 3H_2O$]

The sodium salt of N-chloro.p-toluene sulphonamide is known as Chloramine-T [CAT]. It was first prepared by Chattway.[8] When toluene is allowed to react with chloro-sulphonic acid, it gives ortho and para-toluene sulphonyl chlorides. The para isomer on treatment with ammonia and then with aqueous sodium hypochloride produces Chloramine-T. It can be purified by recystallisation from hot water and then by drying in Air. After successive recrystallisation, the purity of compound is nearly 99.5%. It is difficult to prepare and preserve its anhydrous salt.[9] Hence generally commercially available chloramine-T with 98% purity is used. But it is repeatedly washed with carbon tetrachloride before use.

Solubility of chloramine-T in water is 14 gms in 100 ml at 25^{o} C and 50 gms in 100 ml at 100^{o}C. It is also soluble in alcohol and acetone. The available chlorine content in chloramine-T has been estimated and is found to be 23 to 26%. There are conflicting reports on the stability of chloramine-T in solid state and in solutions.[9]

Dietzel and Taufel[15] reported the decline in assay of 1.4% in 12 months in brown coloured bottle and 5% in clear glass bottle. Chloramine-T solution exposed to sunlight is unstable. So it is protected from sun-light. It is stable for nearly four weeks. The time periods of our experiments are very short. Hence it is safely used.

Chloramine-T is strong electrolyte and it dissociates in aqueous solution as

$$R\text{-}NClNa \rightleftharpoons R\text{-}N\bar{C}l + \overset{+}{N}a$$

where R is the p-toluene-sulphonyl group i.e.

$R = [p\text{-}H_3C.C_6H_4.SO_2]$

The anion then picks up a proton to form a free acid R-NH.Cl

$$R\text{-}NCl^- + H^+ \rightleftharpoons R\text{-}NH.Cl$$

This free acid cannot be isolated but the evidence for existance has been reported.[9] The free acid then gives rise to p-toluene-sulphonamide and dichloramine-T

$$2\ RNHCl \rightleftharpoons R.NH_2 + R.NCl_2$$

The dichloramine-T and free acid after hydrolysis gives hypochlorous acid

$$R\text{-}NCl_2 + H_2O \rightleftharpoons R\text{-}NH.Cl + HOCl$$

$$R\text{-}NHCl + H_2O \rightleftharpoons R\text{-}NH_2 + HOCl$$

Finally HOCl ionizes as

$$HOCl \rightleftharpoons H^+ + \bar{O}Cl$$

$[R = P\text{-}CH_3.C_6H_4SO_2]$

Chloramine-T liberates iodine with acidified potassium iodide solution.

$$R\text{-}N.C\bar{l}.\overset{+}{N}a + 2I^- + 2H^+ \longrightarrow R\text{-}NH_2 + I_2 + NaCl$$

Oxidizing properties of chloramine-T have been well reviewed by many authors.[10-11] It is introduced as an analytical reagent by Null.[12] Thereafter many workers are attracted towards the use of chloramine-T as an oxidising and an analytical reagent. Bishop et al.[9] and Jennings[9-13] have been critically examined chloromine-T as titrametric reagent and standardisation methods.

Chloramine-T is widely used as an oxidising agent in acid medium. A large number of organic and inorganic reducing agents have been estimated by using Chloramine-T as an oxidant by volumetric, potentiometric and amperometric methods. Chloramine-T solution can be standardized by adding potassium iodide solution in presence of (1N)H_2SO_4 and titrating the liberated iodine against standard solution of sodium thiosulphate. The redox potentials of 0.1 M chloramine-T solution saturated with p-toluene-sulphonamide at different pH have been reported by Murthy and Rao[14]. These values are 1.139, 0.778 and 0.614 V at pH 0.65, 7.00 and 9.70 respectively.

c) LITERATURE SURVEY

The kinetics and mechanism of oxidations by chloramine-T have been investigated by many authors. Coull and coworkers[16] were the first to report the kinetics and mechanism of decomposition of Hydrogen peroxide by chloramine-T, in,

Presence of hydrochloric acid. Bernanose and Simons[17] have investigated the oxidation of luminol by chloramine-T in acid medium. Then Pryde and Soper[18] investigated the chlorination of p-cresol by chloramine-T. HOCl formed in the hydrolysis of chloramine-T is supposed to participate in the chlorination of the p-cresol. The kinetics of above reaction was investigated by Higuchi and Hussain.[19]

The oxidation of different types of alcohols (n-butanol, iso-butanol and iso-pentanol) by chloramine-T in acid medium has been studied by Mushran et al.[20] The mechanism proposed involves the hydrolysis of RNHCL giving rise to HOCl, in a slow step, which then reacts with the substrate in the fast step giving rise to the corresponding aldehydes. The rate law is given as,

$$-\frac{d[CAT]}{dt} = k[CAT][H^+]$$

where $[CAT]$ = concentration of chloramine-T.

The oxidation of secondary alcohols (propan-2-ol, butan-2-ol, pentan-2-ol and 1,3 dichloro-propan-2 -ol) by chloramine-T in acid medium has been studied by Natarajan and Thiagarajan.[21] Mahadevappa and Naidu[22] studied the oxidation of unsaturated alcohols by chloramine-T in acid medium, and they show that at low acid concentration the rate law can be given as,

$$-\frac{d[CAT]}{dt} = k[CAT][H^+]$$

and at higher acid concentration[23]

$$\frac{-d[CAT]}{dt} = k[CAT][H^+]^2$$

Kinetics of oxidation of some aldoses by chloramine-T is highly alkaline medium have been studied by Agrawal and Mushran[24] The oxidation rates were found to follow the order,

xylose > arabinose > galactose > mannose

An identical mechanism was proposed by Mushran[25] and coworker for the oxidation of d-ribose by chloramine-T in alkaline medium. Madnawet et al.[26] has studied the oxidation of fructose by chloramine-T in alkaline medium.

Oxidation of phenol and substituted phenols by chloramine-T in aqueous alkaline medium has been reported by Radhakrishnamurti.[27] The reaction was found to be first order in each with respect to substrate and chloramine-T. Electron releasing groups accelerate the rate of the reaction. Oxidation of anisole and substituted anisoles by chloramine-T in aqueous acetic acid medium

has been reported by Murti and Sasmal.[28] They found that below 0.003 M concentration, a fractional order dependence on [anisole] was observed, which then changed to first order at high concentration.

Agrawal, Mushran and Sanehi[29] studied oxidation of formaldehyde and acetaldehyde with chloramine-T using Osmium tetraoxide as catalyst in alkaline medium. The complex formation between chloramine-T and Os(VIII) in a slow step has been assumed . The complex was then supposed to abstract a hydroxide ion from the hydrated form of the substrate in a fast step. The following rate law was suggested

$$\frac{-d[CAT]}{dt} = k \frac{[CAT][OsO_4]}{[OH^-]}$$

The rate law as in agreement with the experimental results.

The kinetics and mechanism of oxidation of ketones has been extensively studied by Mushran[30] et al. They have reported the oxidation of acetone and methyl ethyl ketone by chloramine-T in alkaline medium in the presence of catalyst osmium (VIII) catalyst. Sanehi and coworkers[31] have reported the kinetic investigations of oxidation reactions of chloramine-T with methyl ethyl ketone, diethyl ketone and methyl iso-butyl ketone in a alkaline medium. Formation of 1,2 diketones was reported. Sharma and coworkers[32] studied the kinetics and mechanism of oxidation of methyl iso-propyl, methyl-n propyl and ethyl iso-propyl ketones by chloramine-T in alkaline medium. Naidu and Mahadevappa[33] have studied oxidation of aliphatic

ketones by chloramine-T in acid medium. A rate expression suggested by them is as follow -

$$\frac{-d[CAT]}{dt} = k[CAT][S][H^+]$$

Oxidation of cyclohexanone[34] and cyclopentanone[35] by chloramine-T in alkaline medium has been reported. Singh et al.[36] has reported the oxidation of acetophenone by chloramine-T in aqueous acetic acid medium. In this case enol form of the ketone was supposed to interact with HOCl in the slow and rate determining step.

The kinetics and mechanism of oxidation of amino acids by Chloramine-T has been extensively investigated. For example Mushran and coworkers[37,38] have investigated the kinetics of oxidation of α-amino acids by chloramine-T in alkaline medium. The oxidation of glycine and valine by chloramine-T in hydrochloric acid medium has been reported by Gowda and Mahadevappa.[39] Naidu and coworkers[40] have reported the kinetics of oxidation of leucine, serine, glutamine and glutamic acid by chloramine-T in perchloric acid medium. Kinetics of oxidation of histidine by chloramine-T in alkaline medium has been investigated by Gupta.[41] It is observed from all these investigations that the rate of the reaction decreases with an increase in the pH of the medium. Ionic strength effect is very negligible. Kinetics of oxidation of 2-amino-isobutyric acid by chloramine-T in alkaline medium has been reported by Yadav and coworkers.[42] The mechanism that they have proposed is an interaction between neutral molecule and a charged ion or interaction between two neutral molecules in the slow rate determining step.

Krishnrao[43] has reported the oxidation of Benzoyl hydrazines by chloramine-T in alkaline medium. The order with respect to each [Substrate] and [CAT] is found to be one. The rate is found to be independent of pH. The reaction is accelerated by electron withdrawing groups.

Ramanujan and Triff[44] have reported the kinetic and mechanistic studies of chlorination of anilines. Chlorination of p-toluidine and p-Nitro-aniline has been reported by Murti et al.[45] The mechanism of chlorination is shown to be dipole-dipole type involving direct transfer of chloride from chloramine-T to the substrate.

Mahadevappa and coworkers[46-47] have oxidised dimethyl sulphoxide and diphenyl sulphoxide in perchloric acid, hydrochloric acid and sodium hydroxide media by chloramine-T. Ganapathy and Jayagandhi[48] have reported kinetics of oxidation of Methyl phenyl sulphoxide, m and p substituted phenyl and alkyl sulphoxides in alkaline medium by chloramine-T. A possible mechanism that is suggested involves three rate controlling steps, (i) the reaction between RNHCl ($R\text{-}CH_3C_6H_4SO_2$) and the sulphoxide, (ii) the disproportion of RNHCl and (iii) the reaction between $RNCl_2$ and the sulphoxide. So the mixed order rate is derived.

Banerji[49] has reported the kinetics of oxidation of substituted mandelic acid by chloramine-T in perchloric acid medium. $[ClCH_2]^+$ is assumed to be the reactive species. Singh and coworkers[50] have studied the kinetics of oxidation of α-and β-ketoglutaric acid by chloramine-T in acid medium. A mechanism involves the interaction of enol form of the substrate with chloramine-T in the rate determining step.

Srinivasan and coworkers[51] have reported the kinetics and mechanism of oxidation of phenyl thio-substituted acetic acid by chloramine-T in alkaline medium at pH 10.06. The oxidation proceeds via two paths, the major one, involving RNHCl as the main oxidising species and the minor one involving ClO^- ions. Kinetics and Mechanism of oxidation of lactic acid by chloramine-T catalysed by copper(II) ion, has been reported by Gupta and coworkers.[52]

Mahadevappa and coworkers have reported the detailed investigation of the kinetics of oxidation of thiocyanate ion by chloramine-T in alkaline medium. At low substrate concentration, the rate law is given,

$$\frac{-d[CAT]}{dt} = k \frac{[CAT][NCS]}{[NaOH]^2}$$

which is simplified to

$$\frac{-d[CAT]}{dt} = k [CAT] [NaOH]^{-1}$$

d) OBJECT AND SCOPE OF THE WORK

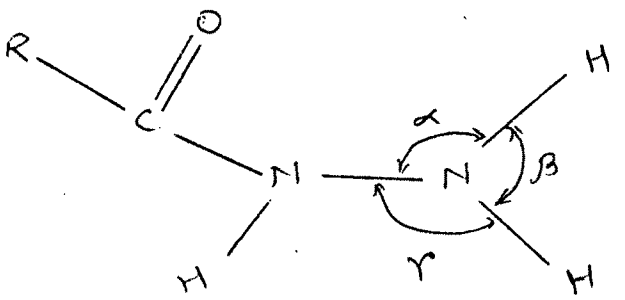
The chemistry of hydrazides is very important and interesting branch of organic chemistry due to the fact that many hydrazides are found to have physiological activity. They have been extensively studied. Since, the discovery of isonicotinic acid hydrazide as a strong anti-tuberculostatic agent.[54] Many derivatives of this compound have been synthesised and tested for anti-bacterial activity.[55-56] Diacyl hydrazine group in certain derivatives of hydra zides has been supposed to be biologically active[57]. Carboxylic acid 1-2 diaryl

hydrazides have been reported to possess anti-inflammatory properties.[58] Isoxazole carboxylic acid hydrazides[59] are active against leprosy and phenothiazine carboxylic acid hydrazide[60] has been reported to have anti convulsive action. Dihydrazides have recently been introduced as antihelminties.[61] Maleic acid hydrazide is used to regulate and inhibit the growth of the plants.[62]. Apart from physiological activity of hydrazides, some of them are important starting materials and intermediates in the synthesis of certain amines, aldehydes and heterocyclic compounds. The Hydrazides are used in heat and corrosive stabilization of cellulose and its derivatives.[63] These are also used as anti-oxidants for polyolefins and polyurethanes, which are otherwise oxidised in presence of copper. An incorporation of hydrazides[64] has improved the applicability in plastics and cable insulations. The small amount of hydrazides is useful in sensitizing electrophotographic layers made up of poly vinyl carbazole.[65] Dihydrazides can be used in cigaratte filters for the selective removal of aldehydes from tobacco smoke. Ion exchange resine for separation of copper, nickel, cobalt, magnessium and transition metal ions have been prepared from co-polymer of 2 methyl-5 Vinyl pyridine and hydrazides of 1-2 ethylene dicarboxylic acid.[66]

The hydrazides are the derivatives of carboxylic acids as well as hydrazine. The preferred nomenclature is to describe any hydrazide as carboxylic acid hydrazide. This nomenclature is also used in chemical abstract. The nitrogen atoms of the hydrazides are designated as 1 and 2 or α and β or N and N^1. The first nitrogen of each pair denotes the nitrogen where the acyl group is inserted.[67] The structure of hydrazide is determined care-

fully by using modern techniques of structure determination. The structure of isonicotinic acid hydrazide has been determined by x-ray crystallography.[68]

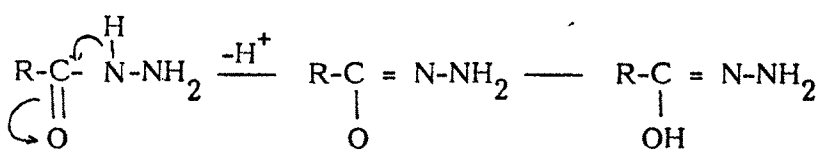
The following diagram gives a reasonable idea about the structure of hydrazide.



$\alpha = 101^{o}$, $\beta = 98^{o}$, and $\gamma = 109^{o}$

The N-N bond length is always between 1.39 and 1.42 A^{o}, which is shorter than in hydrazine which is in between 1.46 and 1.47 A^{o}. This might be due to the formal charge effect and the electron attracting acyl group, which reduces the repulsion between the loan pair of electrons of nitrogen atoms. The C-N bond length is 1.33 A^{o} which is same as in pyridine. This bond, therefore, must acquire roughly a 50% double bond character. The two hydrogen points in the direction of the carbonyl oxygen. All six atoms in the groups lie almost exactly in the same plane.

The hydrazide group is stabilized due to the resonance between amide form (I) and the tautomeric enol form (II) by the shift of a hydrogen atom from nitrogen to the oxygen.



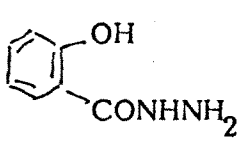
(I) (II)

Due to resonance stabilization of hydrazide group, its basicity is drastically reduced.

The kinetics of oxidation of hydrazides has been investigated by many workers. The oxidation of hydrazides by lead tetracetate leads to the formation of corresponding acids and nitrogen. The oxidation of Benzhydrazides[69] by MnO_2 proceeds through formation of azo-compounds which are solvolysed to corresponding acids.

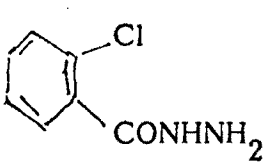
Looking at the survey, it is clear that no complete or sufficient information is available regarding the oxidation of hydrazides by chloramine-T though this reaction is industrially important reaction. So as to get this information completely, I have carried out this work of oxidation of hydrazides by chloramine-T. The hydrazides taken for study are as follows.

(1) Salicylic acid hydrazide (SAH)



and

(2) Ortho-chloro benzoic acid hydrazide [O.CBAH]



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